Nanomedicine

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The term “nanomedicine” is generally interpreted as the application, integration, and translation of nanotechnology to biomedical sciences. Nanomaterials, with a characteristic size ranging between 1 and 100 nm, manifest unique, size-dependent properties in physico–chemical phenomena and can be effectively used to manipulate, measure, stimulate, and perturb a biological system. Over the last decade, a myriad of devices and systems at the nanoscale have been developed for the diagnosis, imaging, and therapy of diseases. These include nanoparticles for the systemic delivery of imaging and therapeutic agents; nano/micro-fluidic systems for organ-on-a-chips; metallic nanoparticles for molecular sensing; electromagnetic nanosensors for the operation and control of medical devices; nanofibers for tissue engineering; and many others.

The large majority of these nanosystems have been developed following a rather empirical approach, while the notion of rationally designing nanostructures, nanodevices, and

nanoparticles has been only recently realized. For instance, in the case of systemic drug delivery, a great variety of nanoparticles have been presented in the literature with different sizes, ranging from a few to several hundreds of nanometers; surface properties, with polymer coatings imparting negative, positive, or neutral electrostatic charges; compositions, including lipids, polymers, carbon, silicon and various metals; and shapes, from the classical spherical to cylindrical, cubical, and discoidal. Is there an optimal combination of size, shape, surface properties, and material compositions that could maximize the accumulation of nanoparticles at the target site (tumor, atherosclerotic plaque, and so on) while minimizing their sequestration in healthy organs? Indeed, similar questions can be posed for the optimization of lab-on-a-chip, scaffolds for tissue engineering, nanosensors, and so on.

The use of computational modeling in the design of nanostructures and nanodevices for biomedical applications would certainly help in optimizing their performance in vivo and in understanding/ predicting the detailed behavior of the biological system, per se. As such, the objective of this special issue is to emphasize the importance of “Computational Nanomedicine” as a critical tool for facilitating the integration of nanotechnology with biomedical sciences. As computational mechanics has already had a profound impact on science and technology over the last decades, we expect that Computational Nanomedicine could have an equally pervasive impact in rationally designing nanostructures, nanodevices, and nanoparticles for biomedical applications.

The manuscripts collected in this special issue touch upon four major topics, namely (i) nanoparticle transport and drug delivery; (ii) cell motility and migration; (iii) multiscale/multiphysics modeling of tumor growth, and (iv) quantification of uncertainty in computational nanomedicine. Specifically, in the contribution by Yaling Liu and col-

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laborators, it is shown how a continuum-based finite element method can be applied to optimize the capture of magnetic nanoparticles by a metallic stent exposed to an external magnetic field in a major blood vessel. Sarkar and colleagues review different mathematical models proposed for describing the mechano-acoustic behavior of echogenic micro/nano-bubbles for biomedical imaging and drug delivery. The manuscript by Decuzzi and colleagues deals with the release of drug molecules from nanoconstructs firmly adhering to the healthy and tumoral vasculature. Continuum mechanics approaches are also used for predicting the spatio-temporal growth of vessel networks and tumor masses in the manuscripts by the groups of Gomez and Schrefler, respectively. In the first contribution, an existing deterministic continuum theory is coupled with a discrete random walk to account for both chemotactic and haptotactic cellular migration in the growth of neo-angiogenic vessels. In the second manuscript, a thermodynamically constrained averaging theory is used to model the tumor and healthy tissue as a multi-phase system, where each phase presents with its specific interfacial tension, viscosity, and adhesion property. The groups of Preziosi and Cavalcanti report on cell adhesion, locomotion, and migration. In Preziosi et al., an extended cellular Potts model is introduced to simulate the active motile behavior of a single cancer cell into narrow

channels built into an artificial polymeric matrix. As an experimental counterpart, the work of Cavalcanti and collaborators investigates the migration of human fibrosarcoma cells in two-dimensional and three-dimensional fibronectin microenvironments. Finally, the two closing contributions address a novel and very critical issue in the computational modeling of natural systems: uncertainty quantification. In biology, independent parameters have rarely fixed values: the blood flow changes with time (pulsatile flow); in space (arteries vs capillaries); and it differs from patient-to-patient, type and stage of the disease. Dealing with such uncertainty is crucial in any design process for nanomedicine. Following this line, Wing Kam Liu and collaborators have first presented a multiscale computational framework, obtained by integrating together all-atomistic simulation, coarse-grained molecular dynamics and the immersed molecular electrokinetic finite element method. The utility of the framework is demonstrated by modeling the assembly, vascular transport, cellular adhesion, and endocytosis of a nanodiamond-based drug delivery platform. Predictions are drawn from the modeling method by quantifying uncertainties in the microcirculation of nanoparticles using a Bayesian updating algorithm. Similarly, in Decuzzi et al., a Bayesian hierarchical model is adopted for predicting the optical conditions for the vascular adhesion of circulating nanoparticles in capillary flow.